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EXAMINER	
GROSS, CHRISTOPHER M	
ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/650,174	PARCE ET AL.	
	Examiner	Art Unit	
	Christopher M. Gross	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *13 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-21,23-27 and 29* is/are pending in the application.

4a) Of the above claim(s) *24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-21,23,27,29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Responsive to communications entered 9/13/2006. Claims 1,3-21,23-27,29 are pending. Claims 24-26 are withdrawn. Claims 1,3-21,23,27,29 are examined herein.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/13/2006 has been entered.

Election/Restrictions

Applicant's election without traverse of invention I (Claims 1-27), drawn to a method of detecting binding activity in the reply filed on 09/12/2005 is again acknowledged.

Species Election

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Each **genus** identified below is indicated in **bold.** Applicant is requested to elect one species from within *each* genus of the elected invention.

(From claims 24-26) **modulator:** applicant is requested to elect a species of detecting binding activity in regard to a modulator being present, as set forth in claims 24-26. Currently claims 1,24-26 are generic for invention I.

The presence of a "modulator" in regard to detecting binding activity is directed to a different process. The related products are patently distinct if the (1) the species as claimed are either not capable of use together or can have a materially different design,

mode of operation, function, or effect; (2) the species do not overlap in scope, i.e., are mutually exclusive; and (3) the species as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the species as claimed have different modes of operation in that the a modulator requires additional materially different steps with regard to measuring enzyme inhibition, for instance, not required for a thorough consideration of the subject matter claimed without a modulator necessarily present. Furthermore, the species as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

Because each of the above species are independent or distinct for the reasons given above, a serious burden on the examiner is created if restriction is not required: a prior art search of each of the species requires a different considerations and additional queries in patent, non-patent and other databases (see MPEP § 808.02). Therein, restriction for examination purposes as indicated is proper.

During a telephone conversation with Ann Petersen on 5/2/2007 a provisional election was made of the method of detecting binding activity without a modulator present with traverse. Affirmation of this election must be made by applicant in replying to this Office action. Claim 24-26 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, **including any claims subsequently added**.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after

the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C.121 is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the prior application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See Transco Prods., Inc. v. Performance Contracting, Inc., 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994) [taken from MPEP 201.01]

The instant application, filed 12/11/2002 is a DIV of 09/579,111 05/25/2000 (now PAT 6,649,358 which claims benefit of 60/155,259 06/01/1999 and claims benefit of 60/176,001 01/12/2000 and claims benefit of 60/176,093 01/14/2000 and claims benefit of 60/191,784 03/24/2000.

Nevertheless, support for the limitation set forth in claim 1 related to detecting a detectable signal that indicates an initial concentration of at least one first component or set of first components prior to entry of the at least one first components or the set of first components into a first channel is not found in the earlier provisional applications. It is further noted that the provisional applications are drawn to methods and devices for detecting transporter activity as opposed to a method of detecting binding activity set forth as the presently claimed subject matter.

Therefore 5/25/2000 is the date for the purposes of prior art concerning claims 1,3-21,23-27,29.

Withdrawn Rejection(s)

The rejection of claims 1, 3, 13-15, 18-20, 21, 23, and 27 under 35 U.S.C. 102(b) as being anticipated by Yager et al. (US Patent 5,716,852) has been withdrawn in view of applicant's amendments to the claims.

The rejection of claims 1, 3, 13-15, 20, 23, and 27 under 35 U.S.C. 102(e) as being anticipated by Wu et al. (US Patent 6,221,677 B1; *effective filling date of 09/26/1997*) has been withdrawn in view of applicant's amendments to the claims.

New Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 recites the limitation "the at least one first component", "the set of first components" each in line 1. The limitation "the first channel" is used throughout claim 29. There is insufficient antecedent bases for each of these limitations in the claim.

In contrast to applicant's remarks, see p 7 (9/13/2006), it is noted that amended claim 29 does not incorporate all the limitations of current claim 1 (i.e. "detecting a detectable signal that indicates an initial concentration of at least one first component or set of first components prior to entry of the at least one first components or the set of first components into a first channel").

New Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,3,5,23,27 are rejected under 35 U.S.C. 102(b) as being anticipated by Weigl et al (1999 Science 283:346-347).

The claimed subject matter per claim 1 is drawn to a method of detecting a binding activity, the method comprising:

(a) detecting a detectable signal that indicates an initial concentration of at least one first component or set of first components prior to entry of the at least one first components or the set of first components into a first channel;

(b-i) flowing the at least one first component or the set of first components through a first channel concomitant with at least one second component or a set of second components,

(b-ii) wherein the at least one first component or the set of first components diffuses more rapidly in solution than the at least one second component or the set of second components, and

(b-iii) wherein the first channel comprises a mixing longitudinal segment, wherein the at least one first component or the set of first components diffuses substantially across the first channel in the mixing longitudinal segment, and

(b-iv) wherein the at least one second component or the set of second components diffuses less than substantially across the first channel in the mixing longitudinal segment,

(b-v) wherein the at least one second component or the set of second components binds to the at least one first component or the set of first components; and

(c) detecting a detectable signal that indicates a final concentration of the at least one first component or the set of first components that remains unbound after exiting from the first channels, thereby demoting the binding activity.

Claim 3 sets forth first components such as a drug.

Claims 4-6 are drawn to various temperatures.

Claims 7-8 set forth various relative speeds for the first component versus the second component.

Claims 9-10 set forth various concentrations fort the first component.

Claims 11-12 set forth various molecular weights for the first component.

Claims 13-14 set forth various diffusional coefficients with regard to the first component.

Claim 15 is drawn to second components comprising receptors, etc.

Claims 16-17 are drawn to various concentrations of the second component.

Claims 18-19 set forth various molecular weights for the second component.

Claim 20 is drawn to fluid direction components such as a fluid pressure force modulator.

Claim 21 is drawn to using the first component solution as a positive control.

Claim 23 is drawn to the first channel being a microchannel.

Claim 27 is drawn to detectable signals such as fluorescence.

Claim 29 is drawn to a method of detecting a binding activity comprising: steps (b) and (c) of claim 1 plus an additional step (d) drawn to flowing the at least one second component or the set of second components through the first channel, thereby providing a negative control for detecting the detectable signal.

Weigl et al teach, throughout the document and especially figure 1, a microfluidic diffusion-based separation and detection method using a "T-sensor" comprising two

channels having a fast diffusing material such as an organic dye (indicator) in one channel and human serum albumin (HSA) loaded in the other channel.

Weigl et al measure fluorescence intensity, with 0 g/100 ml solution of HSA and an indicator (i.e. the indicator control) in figure 2 and is taken as providing detecting a detectable signal that indicates an initial concentration of at least one first component or set of first components prior to entry of the at least one first components or the set of first components into a first channel as set forth in claim 1(a).

Weigl et al teach flowing each channel in parallel in figure 1 which is taken as providing flowing the at least one first component or the set of first components through a first channel concomitant with at least one second component or a set of second components as set forth in claim 1(b-i).

Weigl et al teach in the paragraph bridging columns 2 and 3 on page 346, said small indicator diffuses faster than particles such as a cell, therein reading on the at least one first component or the set of first components diffuses more rapidly in solution than the at least one second component or the set of second components per claim 1(b-ii).

Weigl et al teach as element 7 in figure 7, diffusion of sample analyte (indicator) into the sample stream which reads on first channel comprises a mixing longitudinal segment, wherein the at least one first component or the set of first components diffuses substantially across the first channel in the mixing longitudinal segment per claim 1(b-iii).

Weigl et al disclose minimal diffusion of HSA in figure 2 , thus reading on the at least one second component or the set of second components diffuses less than substantially across the first channel in the mixing longitudinal segment per claim 1(b-iv).

Weigl et al further disclose in figure 2 and the last paragraph on page 346, a change in fluorescence intensity of said indicator upon binding HSA reading on wherein the at least one second component or the set of second components binds to the at least one first component or the set of first components as set forth in claim 1(b-v). Said change in fluorescence intensity is taken as providing detecting a detectable signal as set forth in claim 1(c).

Weigl et al teach in the last paragraph on page 347, said T-sensor may be used in analyzing drugs, reading on claim 3.

Weigl et al teach in the second line in the third column on page 346, room temperature measurements, which is taken as 25 degrees C, as set forth in claim 5.

Weigl et al teach in the first paragraph on page 346 said T-sensor represents a microfluidic device, reading on claim 23.

Said fluorescence measurements according to Weigl et al read on the fluorescence detectable signal of claim 27.

Claims 1,3,7-15,20-21,23,27,29 are rejected under 35 U.S.C. 102(a) as being anticipated by Kamholz et al (1999 Anal Chem 71:5340-5347) as evidenced by Mastro et al (1984 PNAS 81:3414-3418).

Kamholz et al teach, throughout the document and especially figure 1, a microfluidic diffusion-based separation and detection method using a "T-sensor" comprising two channels having the fast diffusing organic dye called AB580 with an affinity for HSA in one channel and HSA alone loaded in the other channel.

Kamholz et al measure fluorescence intensity, with 0 uMolar solution of HSA and an indicator (i.e. the indicator background) in figure 7b-c (at a distance of ca 385 um) and is taken as providing detecting a detectable signal that indicates an initial concentration of at least one first component or set of first components prior to entry of the at least one first components or the set of first components into a first channel as set forth in claim 1(a)

Kamholz et al teach flowing each channel in parallel in figure 1 which is taken as providing flowing the at least one first component or the set of first components through a first channel concomitant with at least one second component or a set of second components as set forth in claims 1(b-i) and 29.

Kamholz et al teach in the paragraph briding the left and right columns on page 5340 small molecules diffuse significant distances and large molecules do not diffuse significantly therein reading on wherein the at least one first component or the set of first components diffuses more rapidly in solution than the at least one second component or the set of second components per claims 1(b-ii) and 29.

Kamholz et al teach an elongated "interdiffusion region" in figure 1 between two sample streams which reads on the first channel comprises a mixing longitudinal segment, wherein the at least one first component or the set of first components

diffuses substantially across the first channel in the mixing longitudinal segment per claims 1(b-iii) and 29.

Kamholz et al disclose minimal diffusion of HSA in figures 1 and 7a-b, thus reading on the at least one second component or the set of second components diffuses less than substantially across the first channel in the mixing longitudinal segment per claim 1(b-iv) and 29.

Kamholz et al further disclose in figure 7c, a change in fluorescence intensity of said AB850 upon binding HSA reading on wherein the at least one second component or the set of second components binds to the at least one first component or the set of first components as set forth in claim 1(b-v). Said change in fluorescence intensity is taken as providing detecting a detectable signal as set forth in claim 1(c) and 29.

Kamholz et al teach in figure 3 flowing the at least one second component or the set of second components through the first channel wherein no binding is observed for HSA and fluroescein, therein providing a negative and positive control, respectively as set forth in claim 29(d) and 21, respectively.

Kamholz et al teach in the last paragraph on page 347, said T-sensor may be used in analyzing drugs, reading on claim 3.

Said AB580 according to Kamholz et al reads on an organic molecule set forth in claim 3.

Kamholz et al teach on page 5246, left column paragraph 4 a diffusional coefficient for AB580 or 4.55×10^{-7} and 6.43×10^{-7} for HSA, which is taken as in the range set forth in claim 7.

Said diffusional coefficient for AB580 is in the range set forth in claims 13-14.

Said diffusional coefficient is taken as being about 10^{-6}, as set forth in claim 14.

Kamholz teach on the right column of page 5341, equations 4 and 5 that the diffusion coefficient is inversely proportional to the viscosity of a solution as well as Stokes radius of a molecule. Therefore, the choice of indicator (fast diffuser), macromolecule (slow diffuser) and solution provides various diffusion speeds. Mastro, for instance in table 3, discloses that the diffusional coefficient of Sorbitol in water is 94 x 10^{-7}, whereas that of Dextran 24,000 in a cell is 1.5 x 10^{-7}, the ratio of which is about 50 as set forth in claim 8.

Kamholz et al teach in figure 5, 5 uMolar AB580, which is in the range set forth in claims 9 and 10.

Kamholz et al teach in the last paragraph on p 5342, AB580 has a molecular weight of 307, in the range set forth in claim 11 and 12. In the same passage, Kamholtz et al teach AB580 has high affinity for HSA, therein HSA is taken as a type of receptor for AB580as set forth in claim 15.

Kamholz et al teach under 'fluidics' on page 5342, the use of a syringe pump, which is taken as a type of fluid pressure force modulator, as set forth in claim 20.

Kamholz et al teach in the first paragraph on page 5340 said T-sensor represents a microfluidic device, reading on claim 23.

Said fluorescence measurements according to Kamholz et al read on the fluorescence detectable signal of claim 27.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1,3-21,23,27,29 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of **Weigl et al** (1999 Science 283:346-347) **or Kamholz et al** (1999 Anal Chem 71:5340-5347) as evidenced by Mastro et al (1984 PNAS 81:3414-3418), each taken separately in view of **Suzuki et al** (1999 JBC 274:31131-31134)

Weigl et al or Kamholz et al is relied on as above.

Note that Kamholz et al teach in figure 5 b 10 uMolar HSA, therein providing the concentration ranges set forth in claims 16 and 17.

Neither Weigl et al or Kamholz et al teach temperatures ranges from about 10 to 40 degrees C (claim 4) or 37 degrees C (claim 6). Neither of Kamholz or Weigl et al

teach an enzyme (claims 16-19) with a molecular weight of 30 kDa (claims 18 and 19).

Suzuki et al, teach throughout the document and especially the abstract the discovery of a 30 kDa SUMO-1 hydrolase enzyme.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to employ the microfluidic diffusion-based separation and detection method using a "T-sensor" per Weigl et al or Kamholz et al to better characterize the SUMO-1 hydrolase of Suzuki et al.

One of ordinary skill in the art would have been motivated to the microfluidic diffusion-based separation and detection method using a "T-sensor" per Weigl et al or Kamholz et al to better characterize the SUMO-1 hydrolase of Suzuki et al because it is of interest to investigate whether SUMO-1 (the substrate for SUMO-1 hydrolase) modification fluctuates in the mammalian cell cycle, as noted by Suzuki et al the last two paragraphs on page 31131.

Furthermore, in accordance with MPEP 2144.05 generally, differences in concentration or temperature, such as those set forth in claims 4 and 6 will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical.

One of ordinary skill in the art would have had a reasonable expectation of success in substituing the SUMO-1 hydrolase of Suzuki et al for the HSA of Weigl et al or Kamholz et al because Weigl et al states that the T-sensor is applicable toward enzymes in the last paragraph on page 347. Therefore it would not have been

unreasonable to apply T-sensor or Weigl et al or Kammolz et al because SUMO-1 hydrolase is an enzyme.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Gross whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on 571 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M Gross
Examiner
Art Unit 1639

cg

J. DOUGLAS SCHULTZ, PH.D.
SUPERVISORY PATENT EXAMINER